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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/510,232	04/11/2005	Barbara Sambuco	260236US0PCT	7049

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EXAMINER	
HAGHIGHATIAN, MINA	
ART UNIT	**PAPER NUMBER**
1616	

NOTIFICATION DATE	DELIVERY MODE
04/17/2008	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/510,232	SAMBUCO ET AL.	
	Examiner	Art Unit	
	MINA HAGHIGHATIAN	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *19-28,30 and 32-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *19-28, 30 and 32-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 01/22/08 has been entered.

Receipt is acknowledged of Amendments and Remarks filed on 12/07/07. Claims 29 and 31 have been cancelled and claims 19 and 42 have been amended. Accordingly, claims **19-28, 30 and 32-44** are pending.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 19-28, 30 and 32-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bernini et al (WO 00/25746).

Bernini et al teach a process for the preparation of suspensions of drug particles for inhalation delivery, said process providing particles of optimized particle size and distribution homogeneously dispersed in the carrier (see abstract). The process is carried out by using a turboemulsifier, optionally followed by a treatment with a high pressure homogenizer. Accordingly, said process includes a first step wherein an aqueous solution which constitutes the carrier is dispersed in a turboemulsifier apparatus. A typical turboemulsifier suitable for the treatment comprises a containment vessel equipped with magnetic stirring and a high potency **turbine** system which is used for **homogenizing the suspension**. The apparatus can also be fitted with a heating jacket as well as a **vacuum** system. In a second step, one or more micronised active ingredients, obtained after conventional milling, are added to the aqueous phase and dispersed in the same turboemulsifier vessel by applying very high speed (2000-3000 r.p.m for 15 to 30 minutes (see page 2, lines 13-32).

Bernini et al also disclose that the mean diameter of at least 90% of the particles is lower than or equal to 5 micron (page 4, lines 5-7). Suitable drugs include beclomethasone dipropionate. The formulations can be prepared by dispersing the active ingredient in an aqueous solution or in a high-boiling organic solvents, such as

alcohols. According to the particle size and particle distribution obtained, they can be used either for **pulmonary** or nasal delivery (see page 7, lines 2-12). It is also stated that the said formulations for inhalation can be advantageously used in the **treatment of** allergic and/or **respiratory disorders such as asthma**, COPD, etc (page 11, lines 18-22).

The resulting suspension can be directly partitioned under sterile conditions, in plastic single-dose containers, pre-formed and sterilized by suitable treatments or produced in sterile by employing the "blow, fill and seal" technology. Additionally, a process for making therapeutically acceptable micronised BDP sterile as a result of gamma-ray irradiation is disclosed (see page 8, lines 15-25).

Tables 1 and 2 show particle size distribution of beclomethasone dipropionate particles, as measured by Malvern apparatus, in both irradiated and non-irradiated formulations. It is shown that the diameter of 90% of the particles can be less than 8 microns or less than 7 microns, diameter of 50% of the particles can be from 2 to 3.5 micron or from 2.5 to 3 microns. Example 1 discloses a process of sterilizing **600 g** of BDP and Example 2 discloses that after loading the apparatus with sterile water for injection, sodium chloride and surfactants are added and the preparation is mixed under magnetic and high potency **turbine** stirring to homogenously disperse the surfactants. The active agent is added to the sterile aqueous base and dispersed under first only magnetic stirring, then with the aid of the turbine system (see page 13).

NOTE: Claim 37 recites a concentration range of 0.01 to 0.1% w/v and claim 42 requires a concentration of 0.04% w/v. Although the said range and amount are not explicitly disclosed by Bernini et al, it is considered that concentration is determined according to the needs of the patient and the capacity of the delivery device as well as other factors.

Resolving the level of ordinary skill in the pertinent art

It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the process for the preparation of an aqueous suspension, as described in Bernini et al '746 reference to effectively and economically prepare the same suspension on an industrial scale. In other words, it would have been obvious to one of ordinary skill in the art to adjust the process going from a pilot to industrial scale production. Additionally, the claims would have been obvious because the technique for improving a particular process was part of the ordinary capabilities of one skilled in the art in view of the teaching of the technique for improvement in other situations (i.e. industrial scale).

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated

by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims **19-28, 30 and 32-44** are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2-9 and 13 of U.S. Patent No. 6,464,958. Although the conflicting claims are not identical, they are not patentably distinct from each other because the instant claims are anticipated by the reference claims. In other words all that is recited in instant claims falls within the scope of reference claims. Specifically the process for the preparation of an aqueous suspension to be used in formulations for inhalation recited in the instant claim 2 comprise the same steps and limitations as the process in reference claims. The active agent, excipients, particle size and particle size distribution, as well as turboemulsifier's limitations are the same or very similar.

Claims **19-28, 30 and 32-44** are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-20 of copending Application No. 10/538,888 (US 20070140980). Although the conflicting

claims are not identical, they are not patentably distinct from each other because the instant claims would have been obvious over the reference claims. The instant claims and the reference claims are drawn to a process for the preparation of aqueous suspension. The difference is that the reference claims recite the process steps of preparing the suspension by employing the device, while the instant claims recite the process steps of device preparing the suspension. However the process steps and the final products are the same and one of ordinary skill in the art would have been able to state the process in either form.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

Applicant's arguments with respect to claims 19-44 have been considered but are moot in view of the new ground(s) of rejection. However, since the pending claims are rejected over the same prior art reference, the arguments will be responded to.

Applicant argues that Document '746 discloses the preparation of an aqueous suspension on the pilot plant scale in which sterilized and micronized BDP is placed in suspension firstly by magnetic stirring and then by turbine stirring at 2600 rpm. Applicant continues that "when this process is applied on the industrial scale, the processing times for achieving homogenization are long, and the dispersions obtained do not have satisfactory homogeneity". Applicant also states that in the claimed process

no magnetic stirring of the particle containing suspension is conducted, but a vacuum is applied. Applicant also argues that "because the micronized active ingredient is passed through the turbine under vacuum, it is possible to obtain finer particles, inside the emulsifier, that have a narrower, more homogenous particle size distribution range with no further need for additional treatments such as the high pressure homogenizer described in '746".

These arguments are not persuasive because one of ordinary skill in the art is capable of adjusting the process steps in any given process to prepare the formulation or product in an industrial scale. Also it is noted that the '746 reference, in Example 1 sterilizes 600 g of BDP and in Example 2, 40 g of BDP is placed in the formulation. It is generally accepted that 600 grams and 40 grams of BDP would be considered "industrial scale" as a normal dosage is in micrograms. Furthermore, '746 teaches, in Example 2, that the excipients and active ingredients are added to the apparatus by magnetic stirring then with the aid of a turbine. '746 discloses that the preparation is mixed under magnetic and high potency turbine stirring to homogeneously disperse the surfactant. One of ordinary skill in the art would be able to adapt the same method for mixing the active agents and prepare a homogenous dispersion.

Applicant makes analogous arguments against the Obviousness Double Patenting rejection because U.S. Patent 6,464,956 is equivalent to '746 reference. Again, the arguments are not commensurate with the scope of claims. Both sets of claims employ the open language of "comprising" and instant claims do not recite any limitation that is not taught by the reference claims. Furthermore, Patent '956 discloses

that vacuum is one of the two options. Modifications to the process would have been obvious to one of ordinary skill in the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MINA HAGHIGHATIAN whose telephone number is (571)272-0615. The examiner can normally be reached on core office hours.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Mina Haghighatian/

Mina Haghighatian
Primary Examiner
Art Unit 1616